In the United States Court of Federal Claims
OFFICE OF SPECIAL MASTERS

Filed: October 25, 2024

DONNA MARTIN,	*	No. 17-1607v
Petitioner,	*	Special Master Sanders
v.	*	
SECRETARY OF HEALTH AND HUMAN SERVICES,	*	
Respondent.	*	

Anne Carrion Toale, Mctlaw, Sarasota, FL, for Petitioner
Neil Bhargava, U.S. Department of Justice, Washington, D.C., for Respondent

DECISION ON ENTITLEMENT[1]

On, October 26, 2017, Donna Martin ("Petitioner") filed a petition pursuant to the National Vaccine Injury Compensation Program ("Program" or "Vaccine Program").[2] Pet. at 1. Petitioner alleges that she received the influenza ("flu") vaccine on November 17, 2014, and as a result, "continues to suffer from fatigue, a neurogenic cough and other sequelae of Microscopic Polyangiitis [("MPA")]." *Id.* at 5.

For the reasons stated below, Petitioner's case is hereby **DISMISSED**.

I. Procedural History

On December 11, 2017, Petitioner filed her medical records, along with a statement of completion. Pet'r's Exs. 1–27, ECF Nos. 8–11. Petitioner filed additional medical records on April 3 and April 26, 2018, along with a second statement of completion. Pet'r's Exs. 30–32, ECF Nos.

[1] This Decision shall be posted on the United States Court of Federal Claims' website, in accordance with the E-Government Act of 2002, 44 U.S.C. § 3501 note (2018) (Federal Management and Promotion of Electronic Government Services). **This means the Decision will be available to anyone with access to the Internet.** In accordance with Vaccine Rule 18(b), a party has 14 days to identify and move to redact medical or other information that satisfies the criteria in § 300aa-12(d)(4)(B). Further, consistent with the rule requirement, a motion for redaction must include a proposed redacted Decision. If, upon review, I agree that the identified material fits within the requirements of that provision, such material will be withheld from public access.

[2] National Childhood Vaccine Injury Act of 1986, Pub.L. No. 99–660, 100 Stat. 3755. Hereinafter, for ease of citation, all "§" references to the Vaccine Act will be to the pertinent subparagraph of 42 U.S.C. § 300aa (2018).

17–18. Respondent subsequently identified additional missing medical records, and Petitioner filed another set of records on July 26 and October 8, 2018. Pet'r's Exs. 33–36, ECF Nos. 23, 25. On October 16, 2018, Respondent filed his Rule 4(c) Report. Resp't's Rept., ECF No. 26.

Petitioner filed an expert report and curriculum vitae with accompanying literature on May 16, 2019. Pet'r's Exs. 37–47, ECF Nos. 36–37. Additional medical records were filed on May 20, 2019. Pet'r's Exs. 48–54, ECF No. 38. Respondent filed his first expert report and medical literature on August 15, 2019. Resp't's Exs. A, Tabs 1–7, B, ECF No. 40. On August 21, 2019, Respondent filed a second expert report, curriculum vitae, and literature. Resp't's Exs. C, Tabs 1–8, D, ECF No. 41. Petitioner filed additional medical records on November 1, 2019, and a supplemental expert report on December 3, 2019. Pet'r's Exs. 56–65, ECF Nos. 43–44. Supplemental responsive expert reports were filed by Respondent on March 11, 2020. Resp't's Exs. E, F, Tabs 1–3, ECF No. 45.

On January 15, 2021, Petitioner filed additional medical records, a supplemental expert report, and medical literature. Pet'r's Exs. 67–81, ECF Nos. 51–52. Respondent filed two additional supplemental expert reports on March 15, 2021. Resp't's Exs. G, H, ECF No. 59. Supplemental expert reports and medical literature were again filed by Petitioner on April 19, 2022, and by Respondent on June 21, 2022. Pet'r's Exs. 82–96, ECF No. 63; Resp't's Exs. I, Tabs 1–20, ECF No. 64. Petitioner then filed his fifth expert report on August 8, 2022. Pet'r's Ex. 97, ECF No. 66. A Motion for Ruling on the Record was filed by Petitioner on February 2, 2023. Pet'r's Mot., ECF No. 74. Respondent responded on March 31, 2023, and Petitioner replied to the response on April 12, 2023. Resp't's Resp., ECF No. 79; Pet'r's Reply, ECF No. 80.

This matter is now ripe for consideration.

II. Evidence

a. Petitioner's Affidavit

Petitioner filed a short affidavit attesting that her claim is appropriate for resolution within the Program. Pet'r's Ex. 28, ECF No. 13-2. She identified her injuries as neurogenic cough, fatigue, and other MPA sequela and asserted that they were all caused by her flu vaccination. *Id.* Petitioner did not provide additional factual information in her affidavit.

b. Medical Records

Petitioner was 56 years old when she received the flu vaccine at issue in this case. Pet'r's Ex. 1 at 1, ECF No. 8-2. Her past medical history was significant for GERD, asthma, allergic rhinitis, anxiety, and obesity. Pet'r's Ex. 25 at 3, ECF No. 10-8. On November 17, 2014, Petitioner presented to her primary care physician, Dr. Johnrose-Brown, for treatment of GERD and weight management. Pet'r's Ex. 23 at 30–33, ECF No. 10-6. Petitioner's physical examination was unremarkable. *Id.* Petitioner received a flu vaccination during that visit. Pet'r's Ex. 1 at 1.

On December 2, 2014, approximately two weeks post vaccination, Petitioner returned to Dr. Johnrose-Brown for head congestion, bilateral ear pressure, nasal drainage, and a cough

ongoing for two weeks. Pet'r's Ex. 23 at 26–28. Petitioner also displayed a bilateral, non-pruritic rash on her upper arms and thighs that had begun a week prior. *Id.* Dr. Johnrose-Brown diagnosed her with a rash consistent with dermatitis and an upper respiratory infection ("URI"). *Id.* Petitioner was prescribed steroid cream and the antibiotic azithromycin. *Id.* On December 8, 2014, Petitioner returned to Dr. Johnrose-Brown for nasal congestion and a cough that was present for one month. *Id.* at 21–23. Dr. Johnrose-Brown diagnosed her with bronchitis, a URI, and started Petitioner on Augmentin, a Medrol dosepak, and tussionex. *Id.*

One week later, on December 15, 2014, Petitioner sought treatment with Lawrence Kass, OD, for blood shot eyes that had been present for five days. Pet'r's Ex. 11 at 5–8, ECF No. 9-3. Dr. Kass diagnosed Petitioner with conjunctivitis. *Id.* On December 18, 2014, Petitioner again returned to Dr. Johnrose-Brown with complaints of nasal congestion and a cough. Pet'r's Ex. 23 at 16–18. Petitioner's chest x-ray was positive for bilateral pneumonia and Petitioner was started on Levaquin. *Id.*; Pet'r's Ex. 6 at 8, ECF No. 8-7. By December 22, 2014, Petitioner reported feeling better with respect to pneumonia, but she complained of a rash present for three weeks when she sought treatment with Dr. Johnrose-Brown. Pet'r's Ex. 22 at 11–14, ECF No. 10-5. Petitioner was diagnosed with skin rash/dermatitis, and Dr. Johnrose-Brown documented that it "could be streptococcal rash if pneumonia is from strep." *Id.* Dr. Johnrose-Brown referred Petitioner to a dermatologist. *Id.* On December 24, 2014, Petitioner sought a dermatology evaluation with Scott Freeman, PA-C at Spencer Dermatology. Pet'r's Ex. 16 at 9, ECF No. 9-8. She complained of a whole body rash that "gradually started." *Id.* at 9–10. On physical examination, Petitioner exhibited a rash on her arms, legs, back, and face. *Id.* She was diagnosed with a non-specific skin eruption and Mr. Freeman documented a "possible drug reaction secondary to flu shot." *Id.* at 10.

On December 30, 2014, Petitioner sought treatment with Dr. Rajesh Agrawal, a pulmonologist. Pet'r's Ex. 24 at 199–200, ECF No. 10-7. Petitioner reported increasing shortness of breath. *Id.* Dr. Agrawal diagnosed Petitioner with acute bronchitis and shortness of breath and ordered labs for further evaluation. *Id.* On December 31, 2014, Petitioner returned to Spencer Dermatology with complaints of a gradual onset, whole body rash. Pet'r's Ex. 16 at 6–8. On physical examination, Petitioner exhibited a macular hyperpigmentation located on the lateral aspects of her upper arms and dorsal thighs. *Id.* Petitioner's skin biopsy revealed a hypersensitivity reaction with histocytes neutrophils and eosinophils located within the dermal layer. *Id.*

On January 13, 2015, Petitioner sought treatment with Jennifer Castro, NP, for an evaluation of a new rash on her legs. Pet'r's Ex. 14 at 5–13, ECF No. 9-6. Petitioner reported that she "had a physical and flu shot before Thanksgiving and started to feel lousy that week." *Id.* Petitioner's ESR and CRP were elevated, and her ANA screen was negative. *Id.* Petitioner was diagnosed with a cough and prescribed steroids. *Id.* On January 15, 2015, Petitioner's chest CT displayed abnormalities. *Id.* at 30–32. On January 19, 2015, Petitioner sought a thoracic surgery consultation with Dr. Suhas Pradhan for suspected pneumonia and a respiratory infection with skin rashes for the last two months. *Id.* at 65. Dr. Pradhan noted Petitioner's upcoming bronchoscopy and indicated that a lung biopsy may be a last resort, if she did not improve. *Id.* On January 20, 2015, Petitioner sought treatment with pulmonologist, Dr. Shenif El Bayadi. *Id.* at 67–70. Dr. El-Bayadi ordered a series of diagnostic testing for further evaluation of Petitioner's symptoms. *Id.*

Petitioner went to St. Joseph's Hospital on January 25, 2015, presenting with cough and blood streaked sputum, dyspnea, and low oxygen levels. Pet'r's Ex. 18 at 2–5, ECF No. 9-10. She was admitted, and a January 29, 2015 medical record noted that Petitioner's "symptoms started in November when she developed a small rash around a flu shot injection site." *Id.* at 19. Petitioner was initially treated with steroids, but she deteriorated and required intubation. *Id.* at 2–5. Petitioner's bronchoscopy cultures were negative and her P-ANCA was positive. *Id.* She was started on plasmapheresis and Rituximab. *Id.* Petitioner also required a blood transfusion. *Id.* Petitioner's condition improved, and she was discharged on February 19, 2015, with the principal diagnoses of acute respiratory failure secondary to alveolar hemorrhage, MPA, hospital acquired pneumonia, and blood loss anemia status-post transfusion. *Id.* At the time of discharge, Petitioner was asymptomatic and ambulating. *Id.*

On February 24, 2015, Petitioner sought follow-up treatment with pulmonologist, Dr. El Bayadi. Pet'r's Ex. 15 at 12–14, ECF No. 9-7. She reported shortness of breath and difficulty with activities of daily living, post hospitalization. *Id.* Dr. El-Bayadi's assessment was Wegener's granulomatosis with vasculitis. *Id.* Dr. El-Bayadi felt Petitioner was clinically stable and instructed her to continue with her current medications. *Id.* Petitioner was also instructed to get the flu vaccine seasonally. *Id.* Petitioner continued treatment with Dr. Dodji Modjinou, a rheumatologist, who followed her during her hospitalization. Pet'r's Ex. 5 at 20–24, ECF No. 8-6. On February 27, 2015, she reported some difficulty going up and down the stairs due to shortness of breath. *Id.* Petitioner was diagnosed with MPA and a purpuric rash. *Id.* On February 28, 2015, Petitioner began in-home physical therapy. Pet'r's Ex. 17 at 37, ECF No. 9-9. Dr. Modjinou saw Petitioner again on March 17, 2015. Pet'r's Ex. 5 at 11–13. Petitioner continued to complain of shortness of breath but was improving. *Id.* On March 25, 2015, Petitioner sought treatment with Dr. El-Bayadi who felt that her MPA had "improved significantly." Pet'r's Ex. 14 at 47–50. Five days later, on March 30, 2015, Petitioner sought evaluation with an ear, nose, and throat ("ENT") specialist, Dr. Lawrence Krieger, for an abnormal sensation in her left posterior pharynx since her extubation. Pet'r's Ex. 3 at 8–12, ECF No. 8-4. Dr. Krieger felt the "symptoms [were] possibly related to reflux, non-acidic reflux, or [a] contact ulcer from prolonged intubation or [a] combination." *Id.* On April 9, 2015, Petitioner was discharged from formal physical therapy and began her home exercise program. Pet'r's Ex. 17 at 113. Petitioner's shortness of breath and fatigue continued, and she returned to Dr. Modjinou on April 23, 2015. Pet'r's Ex. 5 at 2–4. Dr. Modjinou instructed Petitioner to continue her medications and noted that he would "write letter for patient to return to work at 10 hours per week to start, per patient's request." *Id.*

On April 25, 2015, Petitioner presented to urgent care with complaints of left flank pain for one day with an associated one-week history of nausea and vomiting. Pet'r's Ex. 10 at 5–7, ECF No. 9-2. Petitioner was transferred to the emergency room and passed a kidney stone before being discharged the same day. Pet'r's Ex. 18 at 53–55. She returned to her pulmonologist, Dr. Agrawal, on June 2, 2015, with complaints of shortness of breath and sleep problems. Pet'r's Ex. 24 at 40–42. Dr. Agrawal diagnosed Petitioner with shortness of breath, chronic airways obstruction, asthma, and bronchitis and ordered a CT scan. *Id.* Petitioner's CT scan displayed improved ground glass opacities and some evidence of bronchitis and air trapping suggestive of restrictive/obstructive lung disease. Pet'r's Ex. 6 at 13–14.

Dr. Sara Downs became Petitioner's primary care provider on July 8, 2015. Pet'r's Ex. 13 at 14–18, ECF No. 9-5. During that visit, Petitioner reported that she had no active MPA symptoms, and her physical examination was normal. *Id.* On August 14, 2015, Petitioner sought treatment with ENT, Dr. Elisa Lynskey. Pet'r's Ex. 12 at 17, ECF No. 9-4. During that visit, Petitioner complained of a dry, chronic cough associated with hoarseness since her intubation. *Id.* Dr. Lynskey noted that Petitioner's symptoms were likely multifactorial and were a combination of vocal cord irritation and inflammation, as well as acid reflux. *Id.*

On August 17, 2015, Petitioner sought an evaluation with gastroenterologist, Dr. Tejinder Glamour. Pet'r's Ex. 2 at 39–40, ECF No. 8-3. Dr. Glamour ordered an esophagogastroduodenoscopy ("EGD") for Petitioner's ongoing cough and ordered a colonoscopy for preventative screening. *Id.* The EGD revealed esophagitis, and the colonoscopy displayed diverticulosis and hemorrhoids. *Id.* at 15–17. On September 2, 2015, Petitioner returned to Dr. Agrawal and reported that she was not using her CPAP machine, but she continued to experience a cough. Pet'r's Ex. 24 at 22–24. Dr. Agrawal diagnosed her with shortness of breath, obstructive sleep apnea, COPD, mycobacterial disease, and chronic bronchitis and started her on new medications. *Id.*

Continued cough, shortness of breath, and chest pain led to hospitalization for hypoxia from September 21 to September 23, 2015. Pet'r's Ex. 20 at 26, ECF No. 10-3. Her discharge diagnoses included GERD, laryngopharyngeal reflux, mycobacterium avium intracellulare, MPA, and OSA. *Id.* at 29. On October 15, 2015, Petitioner sought treatment with her gastroenterologist, Dr. Glamour, and reported feeling "miserable" and "vomiting up acid." Pet'r's Ex. 2 at 36–37. Dr. Glamour strongly advised Petitioner to discontinue steroids and lose weight to improve her condition. *Id.* On October 23, 2015, Petitioner returned to Dr. Lynskey for evaluation. Pet'r's Ex. 12 at 15. Petitioner felt that her cough and hoarseness symptoms were 80% improved. *Id.* Dr. Lynskey instructed her to continue her acid reflux management as instructed by her gastroenterologist and to return to her office in two months. *Id.*

On November 23, 2015, Petitioner returned to Sara Downs, DO, at her primary care office for a referral to a new gastroenterologist. Pet'r's Ex. 13 at 10–12. Dr. Downs advised her to cease taking NSAIDS and to alter her diet. *Id.* On December 4, 2015, Petitioner sought treatment with Dr. Shilpa Renukuntla, another ENT specialist. Pet'r's Ex. 21 at 5–7, ECF No. 10-4. Dr. Renukuntla diagnosed Petitioner with vocal cord dysfunction and discussed the potential for speech therapy. *Id.* Petitioner returned to Dr. Glamour on December 9, 2015, and reported that she would be starting speech therapy for her vocal cord dysfunction. Pet'r's Ex. 2 at 34. Petitioner's physical examination was normal, and Dr. Glamour instructed her to return for evaluation in six months. *Id.* Following a voice assessment on December 21, 2015, Petitioner was referred for voice therapy. Pet'r's Ex. 21 at 8–11.

Dr. Agrawal considered a surgical vagotomy for Petitioner's ongoing cough during a January 26, 2016 exam. Pet'r's Ex. 24 at 16–18. Dr. Agrawal advised Petitioner to reduce her weight and use her CPAP machine. *Id.* Petitioner returned to Dr. Renukuntla on February 12, 2016, and Dr. Renukuntla again recommended voice therapy. Pet'r's Ex. 21 at 13.

During a March 1, 2016 office visit with Dr. Downs, Petitioner requested diet pills. Pet'r's Ex. 13 at 3–5. Dr. Downs instructed her to seek an evaluation with a weight loss clinic regarding diet pills and to seek a cardiac evaluation. *Id.* On March 21, 2016, Petitioner sought treatment with Dr. Marion Ridley, ENT, for a second opinion. Pet'r's Ex. 21 at 17. Following Petitioner's examination, Dr. Ridley recommended gabapentin and speech therapy. *Id.* On April 19, 2016, Petitioner sought a second opinion with gastroenterologist, Dr. Joel Richter, for her GERD. *Id.* at 19–21. Dr. Richter noted that Petitioner's GERD was well-controlled, and he did not believe GERD was contributing to her cough. *Id.*

On May 16, 2016, Petitioner returned to Dr. Ridley and reported that she "feels cough is much improved, but still coughs when she is around her husband or even speaks to him on the phone. She has seen a psychologist in the past for anxiety. Went for [one] full week without coughing when her husband was away." Pet'r's Ex. 21 at 23–24. Dr. Ridley referred Petitioner to a "psychologist/psychiatrist for anxiety-related cough when around/talking to husband" and referred her to general surgery for a weight-loss surgery consultation. *Id.* On September 23, 2016, Petitioner sought evaluation and treatment with Dr. Michelle Spuza-Milord for lumbosacral spondylosis. Pet'r's Ex. 4 at 10–14, ECF No. 8-5. Petitioner's diagnoses included GERD, lumbosacral spondylosis, and Wegener's granulomatosis with multisystem involvement. *Id.*

In 2017, Petitioner reported that she was interested in bariatric surgery. Pet'r's Ex. 29 at 11–13, ECF No. 15-2. A May 11, 2017 note from an evaluation completed by Dr. Spuza-Milford noted that Petitioner's "pulmonary diagnosis began after last flu shot November 17 2014." Pet'r's Ex. 30 at 20–24, ECF No. 17-2.

c. Petitioner's Expert, Dr. Lindsay Lally, M.D.

Petitioner offered the expert opinion of Dr. Lindsay Lally. Pet'r's Ex. 37, ECF No. 36-2. Dr. Lally received her medical degree from Well Cornell Medical College and completed an internship and residency in internal medicine at New York Presbyterian-Well Cornell. *Id.* She completed an additional fellowship "to focus on research related to vasculitis." *Id.* Dr. Lally has been an assistant professor "within the Scleroderma, Vasculitis and Myositis Center of Excellence at the Hospital of Special Surgery" since 2015. *Id.* She has authored "several articles about different types of vasculitis and ha[s] served as principal investigator in many clinical trials." *Id.* She has treated "more than 100 patients with Antineutrophil Cytoplasmic Antibody (ANCA) Associated vasculitis (AAV)." *Id.*

Dr. Lally agreed with Petitioner's diagnosis of MPA. She explained that MPA is a type of ANCA-AAV "characterized by pauci-immune necrotizing vasculitis of small to medium sized blood vessels and an association with serologically detectable ANCA in the majority of cases." *Id.* Dr. Lally went on to review Petitioner's medical records and provide an overview of an MPA diagnosis. She noted that the rare disease involves "[i]nflammation in the vessels result[ing] in hypoxemia and end organ damage." *Id.* at 2. Using criteria from the 2012 Chapel Hill Consensus Conference, Dr. Lally distinguished MPA from other forms of vasculitis by noting there are "few or no immune deposits" and no granulomatous inflammation, but necrotizing glomerulonephritis and pulmonary capillaritis are common. *Id.* at 3. Additional factors include pulmonary involvement in 85% of patients, specifically, "pulmonary infiltrates or diffuse alveolar

hemorrhage." *Id.* at 4. Dr. Lally noted that Petitioner's medical records indicate she developed sinonasal disease and diffuse alveolar hemorrhage. *Id.* She concluded that Petitioner's "clinical presentation along with the supportive laboratory and radiographic tests are completely consistent with MPA." *Id.*

The pathogenesis of MPA is "not completely understood," but Dr. Lally stated "it is known that there is activation of the innate immune system." *Id.* She explained that one role of the innate immune is the priming of neutrophils in response to the presence of "molecular patterns that may signal 'damage' or 'danger.'" *Id.* Consequently, several pro-inflammatory chemokines are released. *Id.* Dr. Lally continued that "[p]rimed neutrophils are better able to release their toxic granules which have the ability to destroy bacterial invaders in the context of infection." *Id.* In cases of MPA, the neutrophil interaction with antibodies, in the absence of actual bacteria, leads to an autoimmune attack and "endothelial damage." *Id.* at 5. This damage causes the release of more granules, resulting in "more damage to the surrounding blood vessels and tissues," and "more inflammatory cytokine release and more tissue damage." *Id.* Ultimately, "the adaptive immune system with antibody producing B cells and cytokine activating T cells take over resulting in chronic inflammation and scarring." *Id.*

To connect MPA to the flu vaccine, Dr. Lally noted that vasculitis has been reported as an adverse event following flu vaccination. She specifically identified medical "literature of systemic necrotizing vasculitis, such as MPA, occurring after [flu] vaccination." *Id.* at 6 (citing Pet'r's Ex. 46, ECF No. 36-11).[3] In Uji et al. the authors examined a case study involving an 83-year-old woman who received the flu vaccine on November 26, 2003. Pet'r's Ex. 46 at 1. She complained of sore throat and fever seven days later, and worsening symptoms led to her hospitalization on December 11, 2003. *Id.* On the fourth day of hospitalization, the patient was diagnosed with MPA. *Id.* The study noted that infectious agents "are associated with the occurrence of vasculitis, but the precise mechanisms leading to vasculitis after [flu] vaccination are unknown." *Id.* at 4. The authors generally noted that the vaccine could directly cause the inflammation, or the condition could occur as the result of "an immunological activation." *Id.* In the case study, the authors pointed to a decrease in autoimmune inflammatory markers following treatment, possibly "reflect[ing] immunological activity causing vasculitis rather than the direct damage to the vessel walls by the vaccine itself." *Id.* They concluded that "[c]linicians should be aware of the possible association between systemic vasculitis and influenza vaccinations." *Id.* Dr. Lally echoed the authors' disclaimer that "[t]he precise mechanism of vaccine induced MPA is not identified." Pet'r's Ex. 37 at 6. She described complement activation as a mechanism for neutrophil priming leading to "presentation of antigen on the cell surface which could enhance ANCA development and specificity and lead to tissue damage." *Id.*

Although Dr. Lally did not provide a specific onset date for Petitioner's injuries, she opined that "the onset of [Petitioner's] respiratory symptoms on December 2, 2014, establishes a clear temporal relationship between exposure and disease onset." *Id.* Dr. Lally stated that Petitioner's respiratory symptoms were incorrectly related to a "[URI] or an infectious pneumonia in December 2014." *Id.* Instead, Dr. Lally asserted that "these were her presenting features of MPA." *Id.* She noted that this interval is consistent with "a vaccine induced autoimmune response," and concluded

[3] Masoto Uji et al., *Microscopic Polyangiitis After Influenza Vaccination*, 44 INTERNAL MED. 892 (2005).

that Petitioner "developed MPA with pulmonary hemorrhage as a direct result of her [flu] vaccine." *Id.*

In a supplemental report, Dr. Lally acknowledged that Petitioner did have some relevant comorbidities but argued that her vasculitis treatment exacerbated those conditions. Pet'r's Ex. 63 at 1, ECF No. 44-2. She described the potential side effects of Petitioner's corticosteroid, including GERD and chronic infections. *Id.* Dr. Lally clarified that she does not believe Petitioner's MPA was triggered by her phentermine use. *Id.* After noting Petitioner's incomplete treatment history, Dr. Lally conceded that the medication "has definitely been associated with pulmonary arterial hypertension." *Id.* In this case, she argued that Petitioner's elevated pressure "was secondary to intrinsic lung disease related to her MPA, not primary [pulmonary arterial hypertension] as one would see in phentermine toxicity." *Id.* Dr. Lally observed nothing in Petitioner's medical record at the time of vaccination "noting any viral symptoms and no documented physical exam findings consistent with a cold-like illness." *Id.* at 3.

Lastly, Dr. Lally asserted that "[t]here is strong literature to support the role of the innate immune system in AAV/MPA" pathogenesis. *Id.* at 2 (citing Pet'r's Ex. 64, ECF No. 44-3;[4] Pet'r's Ex. 65, ECF No. 44-4).[5] Both the Ohlsson et al. and Brilland et al. papers discuss the role of alternative pathway systems in ANCA-associated vasculitis. The Ohlsson et al. "study shows that primed and ANCA-stimulated neutrophils from AAV patients have a greater ability to activate the alternative complement pathway compared to primed neutrophils from healthy controls." Pet'r's Ex. 64 at 1. The authors were seeking to highlight "the therapeutic potential of C5a[6] and other complement blockade." *Id.* The Brilland et al. study reached a similar conclusion based on animal models and argued that "complement alternative pathway activation has been shown to be determinant in AAV pathogenesis through [] a potent chemoattractant for neutrophils with priming capabilities." Pet'r's Ex. 65 at 1.

Dr. Lally submitted a supplemental expert report to respond to Respondent's experts and further clarify her asserted biological mechanism. Pet'r's Ex. 74, ECF No. 52-1. Noting that the innate immune system is complex, Dr. Lally argued that some parts "may be activated, while others may be actually less effective or dysfunctional, furthering fueling disease." *Id.* at 1. Her and Dr. He's understanding of complement activation's role in AAV disease development are not mutually exclusive. Dr. Lally explained that "the combination of the alternative complement system and the neutrophils is integral to disease development from the triggering of ANCA production through to generation of vasculitic damage," but conceded that "these interactions are not yet clearly defined." *Id.* At the end of the report is a "schematic that depicts the current acceptance of AAV disease pathogenesis in the vasculitis community highlighting the joint interaction between neutrophils

[4] Sophie Ohlsson et al., *Neutrophils from ANCA-Associated Vasculitis Patients Show an Increased Capacity to Activate the Complement System via the Alternative Pathway After ANCA Stimulation*, 4 PLOS ONE e0218272 (2019).

[5] Benoit Brilland et al., *Complement Alternative Pathway in ANCA-Associated Vasculitis: Two Decades Form Bench to Bedside*, AUTOIMMUNITY REVS., https://doi.org/10.1016/j.autrev.2019.102424.

[6] C5a is an anaphylatoxin and chemotactic factor for neutrophils, generated in the cleavage of C5 by C5 convertases. It is a potent local mediator of inflammation. *C5a*, DORLAND'S MED. DICTIONARY ONLINE, https://www.dorlandsonline.com/dorland/definition?id=66271(last visited Oct. 15, 2024).

and complement in perpetuating vascular damage in AAV." *Id.* at 2–3. Dr. Lally also included a chart with the loss of immune tolerance to ANCA antigens and the development of ANCA. *Id.* at 4.

d. Petitioner's Expert, Dr. Marc Serota, M.D.

Dr. Marc Serota graduated from the University of Missouri with a bachelor's degree and medical degree pursuant to an interdisciplinary program. Pet'r's Ex. 82 at 1, ECF No. 63-2. He completed residencies in pediatrics at Cohen's Children's Hospital in New York and in dermatology at the University of Colorado. *Id.* Dr. Serota also completed a fellowship in allergy and immunology at Children's Mercy Hospital in Missouri. *Id.* He is board certified in pediatrics, dermatology, and allergy/immunology. *Id.* Dr. Serota is currently "in private practice in Denver, Colorado [practicing] both Dermatology and Allergy/Immunology." *Id.* at 20. His expertise includes immunology/immunologic mediated disease/skin disease. *Id.*

In his report, Dr. Serota, focused on the biological mechanism that Petitioner asserted and the role of the innate immune system. *Id.* at 6. Dr. Serota explained that the lower oxidative burst capacity in granulocytes seen in MPA patients is only a fair characterization when compared to patients with polyangiitis or eosinophilic granulomatosis. *Id.* This is a comparison of innate immune system activity in individuals that are all suffering from disease without evidence that "MPA does not include a heightened innate immune response" compared to healthy individuals. *Id.* He continued that the Johansson et al. article "discuss[es] the innate immune systems role and changes in the normal homeostasis for patients with AAV including low lymphocytes, increased PMN's . . . , which have an increased release from bone marriage, and increased survival in AAV." *Id.* In fact, Dr. Serota argued that "a drastic reduction in cell lines," is proof to the authors that "that the interplay between the innate and adaptive immune systems and the changes in their homeostasis and release and depletion of their granules, are an important part of autoimmunity." *Id.* Additionally, he cited the Braudeau et al. article to assert that "when the immune system is responding and creating inflammation, some measurables of the immune system will naturally go down as they are used up and brought into tissue – this does not mean they aren't involved." *Id.* at 6–7. Dr. Serota argued that "[i]f those components were not involved in the process, we would expect them to be unchanged." *Id.* at 8. Dr. Serota argued that, in fact, the opposite is true. *Id.* He concluded that the literature "showing decreases in some measurables of the innate immune system ([reactive oxygen species] production and [dendritic cells])" actually supports their involvement and utilization. *Id.*

Dr. Serota also discussed molecular mimicry at length in his expert report. *Id.* at 8–12. He noted that the "etiology of autoimmune disease is not fully elucidated," but a combination of hereditary and environmental factors are likely the main causes. *Id.* at 8. Dr. Serota explained the concept of molecular mimicry by way of mice that developed encephalomyelitis following exposure to hepatitis B. *Id.* at 9. He then listed several diseases that are featured in "numerous articles in the immunologic literature discussing molecular mimicry and when known, the specific human antigen targets being mimicked." *Id.* MPA is not one of those diseases, but Dr. Serota explained, "it is not practical or plausible to study or know every potential molecular target – especially for rare events such as MPA following [flu] vaccination." *Id.* He then spent some time discussing Guillain-Barré syndrome and active infection as catalysts for autoimmunity via molecular mimicry. *Id.* at 10. He asserted that the rare occurrence of MPA does not lend itself to

the best causal evidence ("clinical data, epidemiologic studies, and basic science"), and submitted case reports as "data point[s] we can use to help form an opinion." *Id.* at 10.

Petitioner filed the Kelsall et al.[7] article abstract, which purported to describe a case of MPA following flu vaccination. Pet'r's Ex. 92, ECF No. 63-12. The article text was not filed, but the abstract indicated that patients developed vasculitis, including MPA following "[flu] vaccination or [flu]-like illness." *Id.* The authors contended that "this does not provide conclusive evidence that the vaccination caused the vasculitis, [but] it supports this hypothesis." *Id.*

A second article that Dr. Serota referenced was the Uji et al. article that Dr. Lally also described. Pet'r's Ex. 46. Dr. Serota detailed the patient's clinical progression. Pet'r's Ex. 82 at 11. Following her flu vaccination, the patient developed a fever and sore throat. Pet'r's Ex. 46 at 1. Imaging revealed "thickened bronchovascular bundles, multiple nodules with feeding vessels and consolidation." *Id.* She also had high MPO-ANCA and soluble IL-2R levels in serum, "abnormal renal function and urinary sediment." *Id.* The authors concluded that the decrease of sIL-2r post treatment "might have reflected immunological activity causing vasculitis rather than the direct damage to the vessel walls by the vaccine itself." *Id*. at 4. They acknowledged that while "[s]everal infectious agents, including viruses, are associated with the occurrence of vasculitis, [] the precise mechanisms leading to vasculitis after [flu] vaccination are unknown." *Id.* The authors encouraged clinicians to "be aware of the possible association between systemic vasculitis and [flu] vaccination." *Id.*

Dr. Serota summarized the Konishi et al.[8] article abstract, but the article text was not translated into English from its original Japanese version. Pet'r's Ex. 94, ECF No. 63-14. The abstract noted that the case report involved a 67-year-old female who developed MPA and giant cell arteritis following a flu vaccination. *Id.* at 1. The summary concluded with the assertion "that the [flu] vaccination may cause different types of vasculitis . . . through the common mechanism in pathophysiology." *Id.*

Relying on evidence from case reports is often necessary in instances of vaccine-caused illness, according to Dr. Serota, because these are such rare occurrences of immune system failure. Pet'r's Ex. 82 at 12. He articulated the series of events and failures that must occur within an individual, specifically: 1) the induction of T-cell tolerance to antigens; 2) the presence of genetic pre-dispositions that undermine pathogenesis checkpoints within the immune system; 3) an external trigger; and 4) the failure of T-regulatory cells to stop an autoimmune response. *Id.* Dr. Serota argued that this confluence of events is rare enough as to not pick up a signal on epidemiologic studies even upon millions of doses of vaccine being given. *Id.* He further explained that "[i]t is not enough for an antigen to share homology with human antigens, ALL of these different points of failure must be present." *Id.*

In Petitioner's case, Dr. Serota asserted that there is "a clear temporally associated vaccination," and he agreed "with Dr. Lally's proposed mechanism of autoimmune stimulation."

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[7] J.T. Kelsall et al., *Microscopic Polyangiitis After Influenza Vaccination*, 24 J. RHEUMATOLOGY 1198 (1997).

[8] Mai Konishi et al., *A Case of Microscopic Polyangiitis and Giant Cell Arteritis After Influenza Vaccination*, 34 Japan J. Clinical Immunology 154 (2011).

Id. Dr. Serota concluded that Petitioner's symptoms were likely early symptoms of her MPA and occurred "outside the normal expected timing of a routine viral [URI]." *Id.*

In his final submitted expert report, Dr. Serota did not identify any new arguments or provide further clarification of previously asserted positions. Pet'r's Ex. 97, ECF No. 66-2. He identified areas where he asserted that Dr. He oversimplified or mischaracterized his previous arguments. He also clarified his assertion that in MPA patients, cells within the innate immune system have lower oxidative capacity because that capacity is being used to trigger MPA, whereas in healthy controls the cells are not otherwise being activated and therefor have a larger capacity. *Id.* at 2. Dr. Serota also briefly discussed the difference between wild virus infections and vaccinations, while maintaining that both can be the impetus for autoimmune disease.

e. Respondent's Expert, Dr. Chester V. Oddis, M.D.

Dr. Oddis is a Professor in the Division of Rheumatology and Clinical Immunology at the University of Pittsburgh School of Medicine. Resp't's Ex. A at 1, ECF No. 40-1. He received his undergraduate degree at the University of Pittsburgh and his medical degree at Pennsylvania State University. Resp't's Ex. B at 1, ECF No. 40-7. Dr. Oddis completed his internship and residency at Pennsylvania State and a rheumatology fellowship at the University of Pittsburgh. *Id.* He is board certified in internal medicine and rheumatology and has "managed or consulted on over 100 cases of ANCA-associated vasculitis." Resp't's Ex. A at 1. Dr. Oddis has also written "over 120 peer-reviewed publications and nearly 60 invited articles or book chapters." *Id.* at 2.

Dr. Oddis agreed with Petitioner's treaters and Dr. Lally that Petitioner suffered from MPA. *Id.* at 3. He noted that "clinical features include constitutional symptoms such as fatigue, fever, weight loss, joint pain, sinus problems, pulmonary complaints[,] and kidney or neurologic involvement." *Id.* Petitioner exhibited many of the key features associated with MPA, and Dr. Oddis noted that Petitioner "responded well to the medical treatment" typical for MPA, including "high dose steroids and different forms of immunosuppressive therapy." *Id.* Dr. Oddis continued that Petitioner "had a monophasic course of MPA in that she has not had significant recurrent symptoms for [three] years after this diagnosis." *Id.* at 4.

There was also agreement between Drs. Lally and Oddis that the cause of MPA is largely unknown but involves "activation of the innate immune system." *Id.* However, Dr. Oddis noted "a clear paucity of data and literature support linking any vaccine to the development of systemic vasculitis." *Id.* He opined that there are "other potential alternative explanations" for Petitioner's vasculitis. *Id.* First, Dr. Oddis identified Petitioner's URI with symptom onset "at approximately November 18, which is one day after vaccination." *Id.* He argued that it "[i]t is certainly well known and postulated that an infection can serve as a trigger for many autoimmune and vasculitic illnesses." *Id.* Dr. Oddis also asserted that it is "plausible" that Petitioner's phentermine medication "could have triggered her multisystem illness." *Id.* Specifically, phentermine "belongs to a class of medications termed sympathomimetic amines," and "is known to have vascular effects and in some cases . . . cause pulmonary hypertension." *Id.*

f. Respondent's Expert, You-Wen He, M.D., Ph.D.

Dr. He is a Professor of Immunology at Duke University Medical Center. Resp't's Ex. C at 1, ECF No. 41-1. He received his medical degree from The Fourth Military Medical University in Xian, China and a doctorate in microbiology and immunology from the University of Miami School of Medicine. Resp't's Ex. D at 1, ECF No. 41-10. He also has a master's degree in microbiology and epidemiology from the Academy of Military Medical Sciences in Beijing. *Id.* He has been "conducting research on immunology since 1986." Resp't's Ex. C at 1. Dr. He's research has focused on "both innate and adaptive immunity against viral and bacterial infections," and he has studied "human immune responses to viral infections including [flu]." *Id.* He has served as editor for several major biomedical journals, including the Journal of Immunology and Cell and Molecular Immunology. *Id.*

The lack of epidemiologic evidence to support a relationship between flu vaccination and MPA is Dr. He's main argument against causation in this case. Dr. He noted that the National Academy of Medicine found insufficient evidence "to assess an association between [flu] vaccine and onset of vasculitis." *Id.* at 3. Furthermore, volunteer scientists within the Academy "reviewed mechanistic evidence base on 48 publications reporting or studying onset or exacerbation of vasculitis after administration of the [flu] vaccine [and found evidence was insufficient] for the committee to conclude the vaccine may be a contributing cause of vasculitis." *Id.* Dr. He did concede that there was some evidence of the recurrence of vasculitis symptoms "upon vaccine rechallenge." *Id.* at 4. Specifically, "[a]utoantibodies, T cells, complement activation, and immune complexes may contribute to the symptoms of vasculitis." *Id.* He noted, however, that this evidence was characterized by the Academy Committee as weak, and they ultimately "concluded that the evidence is inadequate to accept or reject a causal relationship between [flu] vaccine and vasculitis." *Id.* Dr. He focused on the lack of associative evidence to opine that the Academy "clearly stated that there is no adequate evidence to support a link between influenza vaccine and MPA." *Id.* Dr. He also discussed "a randomized clinical trial [that] investigated whether [flu] vaccination is safe in patients with ANCA-associated vasculitis." *Id.* The study revealed "no statistically significant increase[d] risk of autoantibody production and disease activity." *Id.*

Dr. He disputed Dr. Lally's contention that an increased innate immune response was observed in MPA patients. He relied on one study of 104 ANCA-AAV patients wherein "[t]he authors found a decreased production of reactive oxygen species in AAV phagocytes and lower oxidative burst capacity in granulocytes" compared to granulomatosis and eosinophilic granulomatosis. *Id.* at 5 (citing Resp't's Ex. C, Tab 6, ECF No. 41-7).[9] Another study conducted by Braudeau et al.[10] found decreased blood dendritic cells in MPA patients during the active phase of disease and a decrease in certain cytokines "when compared to patients in remission and healthy donor controls." *Id.* (citing Resp't's Ex. I, Tab 2, ECF No. 64-3). Dr. He argued that these studies offer support against an innate immune system causation theory. *Id.*

[9] Åsa CM Johansson et al., *Impaired Phagocytosis and Reactive Oxygen Species Production in Phagocytes is Associated With Systemic Vasculitis*, 18 ARTHRITIS RSCH. & THERAPY (2016).
[10] Cécile Braudeau et al., *Dysregulated Responsiveness of Circulating Dendritic Cells to Toll-Like Receptors in ANCA-Associated Vasculitis*, 8 FRONTIERS IMMUNOLOGY (2017).

While Dr. He conceded that there is some "speculation that complement activation could result in enhanced ANCA development and lead to tissue damage," he noted that there is no evidence to support this idea. *Id.* Indeed, all vaccine-induced immune protection develops due to the "activation of the innate and adaptive immu[ne systems] to induce antigen-specific responses." *Id.* In Petitioner's case, Dr. He argued that "no evidence has been provided on the induction of auto-reactive T lymphocytes, complement activation[,] and immune complexes formation [] after her flu vaccination." *Id.* at 6. The temporal relationship of less than one week from flu vaccine to the onset of MPA, "a complex autoimmune disease with autoantibody production," is also too short. *Id.* at 7.

In a supplemental report, Dr. He clarified that the decreased immune function he noted from the Johansson et al. article was observed in comparison to controls. Resp't's Ex. I at 2, ECF No. 64-1. Dr. He wrote, "[i]n fact, the Johansson [et al.] study used healthy human subjects as controls throughout and investigated the activation and functional status of phagocytes between patients and healthy human subjects." *Id.* The authors asserted that "phagocytes in patients with AAV were not more activated than in healthy controls." *Id.* Dr. He agreed with the article's ultimate conclusion that "[t]he association between low reactive oxygen species formation in PMN and disease severity is consistent with findings in other autoimmune diseases and might be considered as a risk factor." *Id.* at 3.

Dr. He also clarified his understanding of the significance of the Braudeau et al. study. *Id.* at 4. The authors noted a significant decrease in "absolute counts of [conventional dendritic cells]," decreases in interleukin production by conventional dendritic cells, and a slight "reduction of TNFα production" in plasmacytoid dendritic cells observed in ANCA-associated vasculitis. *Id.* Dr. He rejected any assertion that these reductions are indicative of "increased recruitment in [inflammatory tissues such as skin, synovial fluids, or muscle." *Id.* (citing Resp't's Ex. I, Tab 2 at 4). This hypothesis, according to Dr. He, "is without evidentiary support." *Id.* Petitioner's expert also claimed that dendritic cells are hyper-activated during remission when they are "no longer needed in the tissue," but that is also disputed by Dr. He. *Id.* at 5.

Petitioner's biological mechanism begins with "activation of innate immunity by [flu] vaccination." *Id.* Dr. He maintained in his supplemental report that innate immune components are suppressed during MPA pathogenesis per the Braudeau et al. study. *Id.* at 6. However, he reiterated that innate and adaptive immunity are necessary to "generate vaccine-induced immune protection." *Id.* Dr. argued that "no evidence has been provided on the induction of autoreactive T lymphocytes, complement activation, and immune complexes formation in [Petitioner] after her [flu] vaccination." *Id.*

Dr. He noted that Petitioner is relying on molecular mimicry to explain how her flu vaccination caused her MPA. Dr. He responded by asserting that "this old theory has been strongly challenged by recent scientific evidence from large sequencing of proteomes of microbial pathogens." *Id.* at 8. Given the extensive peptide similarity between virus and human, "90% of the viral 5-mer peptides are widely . . . repeatedly scattered throughout the human proteome," Dr. He argued that molecular mimicry "would suggest a 100% autoimmune disease rate in the general population after ether infection or vaccination." *Id.* Dr. He noted that even "at the highly stringent 8-mer level, the overlap between viral and human proteome still occurs at 8805 matches." *Id.* The

Institute of Medicine Committee's statement that "homology or even similar conformational structure between an exogenous agent and a self-antigen alone are not sufficient to prove that molecular mimicry is the pathogenic mechanism for disease," is quoted by Dr. He. *Id.* He also noted that sometimes "[c]ross-reacting antibodies can also be secondary to nonspecific tissue injury," and "infection with viruses that express antigens having immunologic cross-reactivity can actually protect against autoimmune disease in certain animal models." *Id.*

Dr. He warned about the conflation of infection-induced immune responses and vaccine-induced immune responses. *Id.* at 9. One major difference that he explained is that "microbial pathogens contain many more [pathogen-associated molecular patterns] to stimulate a much broader immune response than their corresponding vaccines". *Id.* at 10. Furthermore, "[w]ild type virus natural infection routes cannot be controlled, while [a] vaccine is administrated by intramuscular/intradermal/subcutaneous injections that is a controlled process." *Id.* at 11. As it relates specifically to the flu vaccine, Dr. He concluded that "there is no clinical evidence that [flu] vaccine is causally linked to any forms of vasculitis." *Id.* at 14. Instead, Dr. He argued that Petitioner "developed symptoms of nasal congestion, rhinorrhea, and cough," several days post vaccination and was properly diagnosed with a viral URI. *Id.* at 15–16. This infection "would have produced a much stronger immune stimulation than the [flu] vaccination that [Petitioner] received." *Id.* at 16.

III. Summary of the Parties' Arguments

a. Petitioner's Motion for Ruling on the Record

Petitioner's motion for a ruling on the record is a comprehensive briefing that provides a medical history, expert opinion summaries, a legal standard that includes a discussion of plausibility and alternative causation, and an analysis of Petitioner's case pursuant to *Althen*. Pet'r's Mot. (citing *Althen v. Sec'y of Health & Hum. Servs.*, 418 F.3d 1274 (Fed. Cir. 2005)). Petitioner asserted in her legal application section that she should prevail if she "can show by a preponderance of evidence that there is a causal relationship between the vaccine and the injury, whatever the details of the mechanism may be." *Id.* (citing *Moberly v. Sec'y of Health & Hum. Servs.*, 592 F.3d 1315, 1325 (Fed. Cir. 2010). Citing *Moberly*, Petitioner noted that conclusive evidence within the medical literature is not necessary. *Id.* (citing *Moberly*, 592 F.3d at 1325). She also cited *Kottenstette* to assert that a detailed medical and scientific exposition on the biological mechanisms is not required for a causation theory to be sound and reliable. *Id.* (citing *Kottenstette v. Sec'y of Health & Hum. Servs.*, 861 F. App'x 433, 441 (Fed. Cir. 2021)).

Notably, Petitioner sought to address the "significant confusion in the case law as to whether prong one [of *Althen*] can be satisfied by the demonstration of a biologically plausible mechanism." *Id.* at 24. She criticized Respondent's understanding of the phrase and argued that the term "has a specific scientific meaning." *Id.* Petitioner relies on the Reference Manual on Scientific Evidence[11] (within the context of Toxicology) to define the term as "consideration of existing knowledge about human biology and disease pathology to provide a judgement about the

[11] National Academies of Sciences, Engineering, and Medicine. 2011. Reference Manual on Scientific Evidence: Third Edition. Washington, DC: The National Academies Press. https://doi.org/10.17226/13163.

plausibility that an agent causes disease." *Id.* The the authors note that "summing, or synthesizing, data addressing different linkages [between kinds of data] forms a more complete causal evidence model and can provide the biological plausibility needed to establish the association being advocated or opposed." *Id.* at 23–24. (internal quotations omitted). Petitioner argued that scientific and medical definitions of biological plausibility are consistent with a Program application that the concept is "not only relevant [] in any discussion of vaccine causation, but its existence lends credence to an inference of causality." *Id.* at 25. Lastly, Petitioner referenced several cases to argue that "[w]ell established vaccine precedents refer to 'proof of medical plausibility." *Id.* at 26.

Petitioner next sought to establish how to determine if a causation theory is reliable, specifically as it relates to molecular mimicry. She noted that molecular mimicry "has been accepted as a sound and reliable theory, even without demonstrating specific homology between a vaccine and the autoimmune injury, in some cases." *Id.* at 29. Petitioner noted that there is no need for epidemiological studies to prove causation as that would "impermissibly raise the [P]etitioner's burden of proof." *Id.* at 30. Petitioner went on to discuss her burden pursuant to the remaining *Althen* prongs.

In the analysis section of her motion, Petitioner reiterated the biological mechanism discussed by her experts, Drs. Lally and Serota. She provided a diagram that explains the interplay among genetic predispositions, environmental factors, and characteristics of the innate and adaptive immune systems that is key to the pathogenesis and propagation of ANCA-AAV. *Id.* at 41. She also provided a flowchart to "elucidate the key stages in ANCA-AAV," from the initial loss of immune tolerance to ANCA antigens, to the role of activated neutrophils in causing inflammation, leading to necrotizing vasculitis and scarring. *Id.* at 43.

Molecular mimicry is the mechanism submitted by Petitioner to explain how vaccination results in the loss of ANCA tolerance. She noted that "molecular mimicry and an association of this phenomenon with antigenic stimuli from both de novo infection and from vaccination are well established in the scientific literature." *Id.* at 44. Petitioner then acknowledged a previously brought claim that unsuccessfully "offered the theory of molecular mimicry to prove the [flu] vaccine caused her MPA." *Id.* at 45 (citing *Knorr v. Sec'y of Health & Hum. Servs.*, No. 15-1169V, 2018 WL 6991548 (Fed. Cl. Spec. Mstr. Dec. 7, 2018)). In that case, Petitioner noted the Chief Special Master required "some evidence that the ANCA antibodies that drive the resulting vasculitis are produced as a result of vaccination." *Id.* at 46 (quoting *Knorr*, 2018 WL 6991548, at *29). The expert's lack of familiarity with ANCA-AV was also of concern in the prior case. *Id.* Petitioner argued that her case is distinguishable because she has offered a vasculitis expert, and she did not rely on medical literature that only discussed granulomatosis with polyangiitis (GPA), a different type of ANCA-AV than MPA, at issue in both cases.

In the present case, Petitioner presented case studies of "systemic necrotizing vasculitis, such as MPA, occurring after [flu] vaccination." *Id.* at 57. She conceded that the causation mechanism is not identified but noted one theory of "upregulation of the immune response after the vaccine [leading] to an exuberant host response inappropriately resulting in autoantibody production and disease propagation." *Id.* This immune system response necessarily involves complement activation that "could result in neutrophil priming" and initiate MPA pathogenesis. *Id.*

Petitioner stated that case studies do not provide conclusive evidence that the flu vaccine can cause MPA; however, "together with the serologic data [presented], it supports the hypothesis." *Id.* at 60. Through her medical literature filings and expert opinions, Petitioner argued that she presented "evidence of antibody responses specifically localized to the affected joint" to support a theory of molecular mimicry, "and also demonstrate[d] that autoimmune responses can be localized to the target tissues, and not necessarily found in serum in all instances." *Id.*

With respect to *Althen* prongs two and three, Petitioner argued that "the medical records show a clinical course consistent with the mechanism and time frame within which MPA can occur following vaccination. *Id.* at 61. Drs. Lally and Serota opined that her cold-like symptoms that were diagnosed as a URI, "were more likely the presenting symptoms of her MPA." *Id.* They noted that her symptoms were "outside the normal expected timing of a routine viral [URI]," but the onset was within days of her vaccination. *Id.* Dr. Serota also highlighted her lack of documented cold symptoms on the day of vaccination. *Id.* Lastly, Dr. Serota pointed to Petitioner's "elevated ANCA IgG, perinuclear pattern with increased myeloperoxidase." *Id.* Petitioner did not articulate an appropriate timeframe for a medically acceptable temporal relationship between her vaccination and the onset of her MPA. However, she noted Dr. Lally's opinion that the "interval between [vaccination and onset of a week] is consistent with the timeline that one would expect from a vaccine induced autoimmune response." *Id.* (citing Pet'r's Ex. 82 at 12).

Finally, Petitioner addressed Respondent's contention that there were potential alternative causes for her MPA. *Id.* at 63–64. She reiterated Dr. Serota's position that a URI is inconsistent with her clinical presentation in onset and duration. *Id.* at 63. Dr. Lally dismissed Respondent's contention that Petitioner's use of phentermine was the cause of her MPA. *Id.* at 64. While he acknowledged that phentermine has been associated with pulmonary arterial hypertension (PAH), Dr. Lally argued that Petitioner's was secondary to intrinsic lung disease related to her MPA, not primary PAH as one would see in phentermine toxicity. *Id.*

b. Respondent's Response

Respondent's response to Petitioner's motion included procedural and medical histories, a section outlining the applicable legal framework, and an argument that Petitioner has not met her burden to "establish[] a causal link between the alleged injury and a covered vaccine." Resp't's Resp. at 27. In Respondent's discussion of Petitioner's *Althen* prong one evidence, he noted that "the Federal Circuit has made clear that 'simply identifying a plausible theory of causation is insufficient for a petitioner to meet her burden of proof." *Id.* at 16 (citing *LaLonde v. Sec'y of Health & Hum. Servs.*, 746 F.3d 1334, 1339 (Fed. Cir. 2014)). Both parties agree that Petitioner "was properly diagnosed with MPA." *Id.* at 17. Respondent asserted that "[t]he exact mechanism of disease remains unclear, but genetics and infection may be associated with MPA disease development." *Id.* (internal quotations omitted). According to Respondent, Dr. Serota's contention that MPA is too rare an event to identify "every potential molecular target," is insufficient because shared homology is very common and autoreactive T cells are present in many healthy individuals. *Id.* at 18. Therefore, those two events are not indicative of disease. *Id.* Respondent argued that there is insufficient epidemiological evidence to "assess an association between [flu] vaccine and onset of vasculitis." *Id.* at 19 (citing IOM, 2012).

Likewise, a study of "the mechanistic evidence between the flu vaccine and MPA [was] inadequate to accept or reject a causal relationship." *Id.* Dr. He argued that a study of ANCA-AAV patients did not reveal a "statistically increased risk of autoantibody production and disease activity following flu vaccination." *Id.* at 19. Isolated case studies "do not provide evidence beyond temporality." *Id.* Respondent also reiterated the significance of studies showing the decreased production of reactive oxygen species, dendritic cells, and relevant cytokines. Dr. He argued that these studies "argue against the activation of innate immunity theory" and ultimately, Petitioner's theory of causation. *Id.* at 21. Respondent asserted that generally, "newer research [] casts doubt on the wide applicability of [molecular mimicry], given that viral and human proteomes have massive peptide sharing." *Id.* He continued that Petitioner has not provided the additional medical and scientific evidence to support her theory that "ANCA antibodies that drive the resulting vasculitis are produced as a result of vaccination." *Id.* at 22 (internal citations omitted). Petitioner's expert is a rheumatologist that accurately diagnosed Petitioner; her MPA is undisputed. Respondent argued that "Dr. Lally has simply not shown the scientific heft required as a causation expert." *Id.*

Respondent argued that Petitioner has not met her burden under the second prong of *Althen* because her treaters maintain that Petitioner suffered from a URI, "a well-known trigger for vasculitic disease." *Id.* at 24. Respondent further argued that Petitioner has not met her burden under *Althen* prong three. *Id.* Specifically, Respondent asserts Petitioner is "perhaps intentionally vague, as her assertion that her earliest URI symptoms arising right after vaccination were actually MPA is inconsistent with the multi-step innate and adaptive immune responses she has proposed." *Id.* at 25–26. Because Petitioner has not established a prima facie case of causation, Respondent bears no burden of proof in this case. *Id.* at 26.

IV. Applicable Law

I am resolving Petitioner's claim on the filed record. The Vaccine Act and Rules not only contemplate but encourage special masters to decide petitions on the papers where, in the exercise of their discretion, they conclude that doing so will properly and fairly resolve the case. *See* 42 U.S.C. § 12(d)(2)(D); Vaccine Rule 8(d). The decision to rule on the record in lieu of a hearing has been affirmed on appeal. *Kreizenbeck v. Sec'y of Health & Hum. Servs.*, 945 F.3d 1362, 1366 (Fed. Cir. 2020); *see also Hooker v. Sec'y of Health & Hum. Servs.*, No. 02-472V, 2016 WL 3456435, at *21 n.19 (Fed. Cl. Spec. Mstr. May 19, 2016) (citing numerous cases where special masters decided cases on the papers in lieu of hearing and those decisions were upheld). I am simply not required to hold a hearing in every matter, no matter the preferences of the parties. *Hovey v. Sec'y of Health & Hum. Servs.*, 38 Fed. Cl. 397, 402–03 (1997) (determining that the special master acted within his discretion in denying an evidentiary hearing); *Burns v. Sec'y of Health & Hum. Servs.*, 3 F.3d 415, 417 (Fed. Cir. 1993); *Murphy v. Sec'y of Health & Hum. Servs.*, No. 90-882V, 1991 WL 71500, at *2 (Fed. Cl. Spec. Mstr. Apr. 19, 1991).

To receive compensation under the Vaccine Act, a petitioner must demonstrate either that: (1) the petitioner suffered a "Table injury" by receiving a covered vaccine and subsequently developing a listed injury within the time frame prescribed by the Vaccine Injury Table set forth at 42 U.S.C. § 300aa-14, as amended by 42 C.F.R. § 100.3; or (2) the petitioner suffered an "off-

Table injury," one not listed on the Table, as a result of his receiving a covered vaccine. *See* 42 U.S.C. §§ 300aa-11(c)(1)(C); *Moberly v. Sec'y of Health & Hum. Servs.*, 592 F.3d 1315, 1321 (Fed. Cir. 2010); *Capizzano v. Sec'y of Health & Hum. Servs.*, 440 F.3d 1317, 1319–20 (Fed. Cir. 2006). Petitioner does not allege a Table injury in this case; thus, she must prove that her injury was caused-in-fact by a Table vaccine.

In the seminal case of *Althen*, the Federal Circuit set forth a three-pronged test used to determine whether a petitioner has established a causal link between a vaccine and the claimed injury. *See* 418 F.3d at 1278–79. The *Althen* test requires petitioners to set forth: "(1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of a proximate temporal relationship between vaccination and injury." *Id.* at 1278.

Each of the *Althen* prongs requires a different showing. Under *Althen* prong one, petitioners must provide a "reputable medical theory," demonstrating that the vaccine received *can cause* the type of injury alleged. *Pafford v. Sec'y of Health & Hum. Servs.*, 451 F.3d 1352, 1355–56 (Fed. Cir. 2006) (citations omitted). To satisfy this prong, a petitioner's theory must be based on a "sound and reliable medical or scientific explanation." *Knudsen v. Sec'y of Health & Hum. Servs*., 35 F.3d 543, 548 (Fed. Cir. 1994). Such a theory must only be "legally probable, not medically or scientifically certain." *Id.* at 549.

Petitioner may satisfy the first *Althen* prong without resorting to medical literature, epidemiological studies, demonstration of a specific mechanism, or a generally accepted medical theory. *Andreu v. Sec'y of Health & Hum. Servs.*, 569 F.3d 1367, 1378–79 (Fed. Cir. 2009) (citing *Capizzano*, 440 F.3d at 1325–26). This may be accomplished in a number of ways. "Reliability and plausibility of . . . pathogenesis can be bolstered by providing evidence that at least a sufficient minority in the medical community has accepted the theory, so as to render it credible." *See Pafford v. Sec'y of Health & Hum. Servs.*, No. 01-0165V, 2004 WL 1717359, at *4 (Fed. Cl. Spec. Mstr. July 16, 2004). Special Masters, despite their expertise, are not empowered by statute to conclusively resolve what are complex scientific and medical questions, and thus scientific evidence offered to establish *Althen* prong one is viewed "not through the lens of the laboratorian, but instead from the vantage point of the Vaccine Act's preponderant evidence standard." *Andreu*, 569 F.3d at 1380.

The second *Althen* prong requires proof of a logical sequence of cause and effect, usually supported by facts derived from a petitioner's medical records. *Althen*, 418 F.3d at 1278; *Andreu*, 569 F.3d at 1375–77. The third *Althen* prong requires establishing a "proximate temporal relationship" between the vaccination and the injury alleged. *Althen*, 418 F.3d at 1281. That term has been equated to the phrase "medically-acceptable temporal relationship." *Id.* A petitioner must offer "preponderant proof that the onset of symptoms occurred within a timeframe which, given the medical understanding of the disorder's etiology, it is medically acceptable to infer causation." *de Bazan v. Sec'y of Health & Hum. Servs*., 539 F.3d 1347, 1352 (Fed. Cir. 2008). The explanation for what is a medically acceptable timeframe must also coincide with the theory of how the relevant vaccine can cause an injury (*Althen* prong one's requirement). *de Bazan*, 539 F.3d at 1352; *Shapiro v. Sec'y of Health & Hum. Servs*., 101 Fed. Cl. 532, 542 (2011), *recons. denied after remand on other grounds*, 105 Fed. Cl. 353 (2012), *aff'd without op.,* 503 F. App'x 952 (Fed. Cir. 2013);

Koehn v. Sec'y of Health & Hum. Servs., No. 11-355V, 2013 WL 3214877 (Fed. Cl. Spec. Mstr. May 30, 2013), *mot. for review denied* (Fed. Cl. Dec. 3, 2013), *aff'd*, 773 F.3d 1239 (Fed. Cir. 2014). The special master cannot infer causation from temporal proximity alone. *See Thibaudeau v. Sec'y of Health & Hum. Servs.*, 24 Cl. Ct. 400, 403–04 (1991); *see also Grant v. Sec'y of Health & Hum. Servs.*, 956 F.2d 1144, 1148 (Fed. Cir. 1992).

A petitioner who satisfies all three prongs of the *Althen* test has established a prima facie showing of causation. *Hammitt v. Sec'y of Health & Hum. Servs*., 98 Fed. Cl. 719, 726 (2011). When and if a petitioner establishes a prima facie case, the burden then shifts to the government to prove that an alternative cause, unrelated to the administration of the vaccine, was the "sole substantial factor" in causing the alleged injury. *de Bazan*, 539 F.3d at 1354; *see also Hammitt*, 98 Fed. Cl. at 726 (explaining that the respondent's burden is to show that the "factor unrelated" was the "sole substantial factor" in causing the injury). Additionally, a factor unrelated "may not include 'any idiopathic, unexplained, unknown, hypothetical, or undocumentable cause, factor, injury, illness or condition.'" 42 U.S.C. § 300aa-13(a)(2).

In Program cases, contemporaneous medical records and the opinions of treating physicians are favored. *Capizzano*, 440 F.3d at 1326 (citing *Althen*, 418 F.3d at 1280). This is because "treating physicians are likely to be in the best position to determine whether 'a logical sequence of cause and effect show[s] that the vaccination was the reason for the injury.'" *Id.* In addition, "[m]edical records, in general, warrant consideration as trustworthy evidence. The records contain information supplied to or by health professionals to facilitate diagnosis and treatment of medical conditions. With proper treatment hanging in the balance, accuracy has an extra premium. These records are also generally contemporaneous to the medical events." *Cucuras v. Sec'y of Health and Hum. Servs.*, 993 F.2d 1525, 1528 (Fed. Cir. 1993). While a special master must consider these opinions and records, they are not "binding on the special master or court." § 13(b)(1). Rather, when "evaluating the weight to be afforded to any such . . . [evidence], the special master . . . shall consider the entire record . . . ." *Id.*

In determining whether a petitioner is entitled to compensation, a special master must consider the entire record and is not bound by any particular piece of evidence. § 13(b)(1) (stating that a special master is not bound by any "diagnosis, conclusion, judgment, test result, report, or summary" contained in the record). Furthermore, a petitioner is not required to present medical literature or epidemiological evidence to establish entitlement. The special master essentially must weigh and evaluate opposing evidence in deciding whether a petitioner has met their burden of proof. *Andreu v. Sec'y of Health & Hum. Servs.*, 569 F.3d 1367, 1380 (Fed. Cir. 2009); *see also Grant v. Sec'y of Health & Hum. Servs.*, 956 F.2d 1144, 1149 (Fed. Cir. 1992).

V. Analysis

a. General Causation: *Althen* Prong One

There is no dispute in this case that Petitioner suffers from ANCA-AAV, specifically MPA. MPA is a type of small vessel vasculitis with most patients also presenting with necrotizing glomerulonephritis and/or diffuse alveolar hemorrhage. There is also no dispute that the pathogenesis of MPA is unclear. It is an autoimmune disease, characterized by the presence of

antineutrophil cytoplasmic autoantibodies. The experts agree that the innate immune system is involved but differ as to context. The disconnect concerns what, if any, relationship exists among vaccination, innate system reaction, and ANCA-AAV.

Petitioner's expert Dr. Lally and Respondent's expert Dr. Oddis both agree that innate immune system activation plays a role in MPA pathogenesis. Dr. Lally argued that that this activation manifests as an alternate complement system that results in increased ANCA antigen production and ultimately, vasculitis. Dr. Oddis did not rebut Dr. Lally's characterization of the alternative complement system as a catalyst for MPA. He noted that this is not a causation theory and focuses on etiology without pathology. Respondent's second expert, Dr. He, argued that there is no evidence of increased innate system activity in cases of MPA, particularly given the decreased reactive oxygen species production and dendritic cells in patients. Alternatively, Petitioner's second expert, Dr. Serota, argued that when innate system measurables in AAV patients are used and brought into tissue, a natural result is decreased levels, but this is evidence of active involvement in MPA pathogenesis. Either of these theories could occur in a patient, and there is no way of knowing in any given case if, for example, dendritic cells are depleted due to decreased production or extensive use. Even if the former is true, that does not disqualify Dr. Lally's point that the alternative complement system plays a role in the development of vasculitis. Experts on both sides have agreed that the innate system is involved in this process, and Dr. Lally has explained how the alternative complement system produces a feedback loop, resulting in progressive vasculitis. Petitioner has presented preponderant evidence that the innate system is involved in the development of MPA, but the inquiry does not end there.

Dr. Lally is an esteemed vasculitis expert who clearly explained Petitioner's diagnosis and presentation. She is not, however, an immunologist. Dr. Lally relied heavily on a single case study to establish that vasculitis can follow vaccination but conceded that the specific mechanism is unclear. Conversely, Dr. Oddis argued that Dr. Lally presented no direct evidence that links a post-vaccination, innate system response to vasculitis. He noted the lack of data and literature to support Petitioner's position and did not address Dr. Lally's argument any further. Success in this Program does not depend upon epidemiological studies or medical literature that proves a medical or scientific theory. However, Petitioner's mechanism must consist of a sound and reliable theory, not simply plausible conclusions.

In her brief, Petitioner included a comprehensive discussion on the significance of mechanism plausibility to meet the preponderant standard. Petitioner reiterated the Federal Circuit's admonition that the applicable standard of proof is not certainty or convincing evidence. Instead, she argued that "more likely than not" is akin to the meaning of biological plausibility within the medical and scientific communities. Petitioner is correct that biological plausibility is a solid foundation upon which to build a theory that is sufficiently substantiated, competent, and reliable. The Reference Manual on Scientific Evidence also assesses the value of medical evidence based on the ability to consistently repeat study findings. Given the rarity of some of the conditions that are routinely seen in the Program, this covariant of plausibility may not be a realistic requirement for a successful vaccine claim. The Federal Circuit has held repeatedly that "*Althen* makes clear that a claimant's theory of causation must be supported by a reputable medical or scientific explanation." 418 F.3d at 1278. A comprehensive evaluation of medical testimony,

specifically medical causation theories, should be used in the Program to ensure experts substantiate their opinions or provide reliable support for their conclusions.

Petitioner distinguished her case from a prior, unsuccessful MPA claim by noting that she (1) obtained a vasculitis expert that could discuss MPA specifically; (2) established that MPA is an autoimmune disease characterized by the presence of autoantibodies and a localized immune response in support of molecular mimicry; and (3) presented a case study that discusses a patient who developed MPA following vaccination to establish an appropriate timeframe and clinical progression. Indeed, Petitioner's vasculitis expert effectively explained and confirmed her diagnosis. However, her diagnosis was never in dispute, given her medical records. Also not in dispute is MPA's autoimmune nature. Autoimmune conditions are some of the most common types of injury alleged in the Program due to their direct relationship to the immune system, the bodily system that is targeted by vaccines. Dr. He explained that the innate immune system (and adaptive immunity) is a necessary condition to "generate vaccine-induced immune protection." Resp't's Ex. I at 6. Indeed, anytime the body is introduced to a foreign antigen, the immune system is activated as a direct responder. While it is true that autoimmune diseases and molecular mimicry both result from immune system dysfunction, that per se does not establish the two are connected in every instance. Lastly, while case reports are a common type of evidence used when trying to determine etiology in rare occurrences, isolated case reports are largely unhelpful beyond identifying a correlation that could be the basis for further study. Petitioner may have distinguished her case from previous unsuccessful claims, but she must still provide preponderant evidence of flu vaccine causation for MPA.

Petitioner's immunology expert, Dr. Serota, fleshed out this asserted causation theory. He linked Dr. Lally's discussion of MPA pathogenesis to vaccine immunogenicity through molecular mimicry. Dr. Serota acknowledged the impartibility and implausibility of discovering the homology for an event as rare as MPA. He referenced a second case study, but only the abstract was filed for my consideration. Of note, the authors provided a disclaimer that the study only provided support for the hypothesis that vaccines can cause vasculitis. Without additional context, the abstract's evidentiary value is minimal. Dr. Serota devoted a significant percentage of his report to a discussion of molecular mimicry. However, his explanation was foundational and did not address the specific characteristics of MPA or how the flu vaccine specifically is a potential mimic. Dr. Serota did not clarify why he chose to use mice that developed encephalitis after hepatitis B exposure as a way of illustration in this case that does not involve a brain injury or hepatitis.

Dr. He argued on Respondent's behalf that recent studies focused on molecular mimicry have illustrated the widespread prevalence of peptide homology. Indeed, if molecular mimicry was as common statistically as one would expect given the level of homology naturally present among living things, every person vaccinated or subject to an infection could at some point develop an autoimmune disease. Dr. He also cited the Institute of Medicine's statement that homology is insufficient to prove a molecular mimicry pathology for a disease. Although the Program does contemplate rare conditions that may not appear in widespread studies, molecular mimicry is commonly submitted in cases as a causation theory without any specificity to the vaccine administered or the injury alleged. Additionally, Dr. He correctly noted how studies that focus on molecular mimicry post infection are conflated with vaccine causation, even in cases where the immune response is much weaker from the vaccine than the wild virus. Due to the ever-growing

body of literature that illustrates "the overlap between viral and human proteome," Petitioner must provide preponderant evidence that narrows her theory of causation to her alleged vaccine and injury. She does not do that. Petitioner has not presented preponderant evidence of a medical theory that causally connects the flu vaccine to the development of MPA.

b. Specific Causation: *Althen* Prong Two

Because Petitioner has not presented preponderant evidence of a legally probable causation theory, I cannot determine if a logical sequence of cause and effect exists in her case. In support of their argument for vaccine causation in this case, Drs. Lally and Serota both opined that Petitioner's cold-like symptoms were misdiagnosed as a URI instead of the onset of her MPA. Petitioner's treaters, including the primary care physician who saw her first post vaccination, a pulmonologist, and a thoracic surgeon, all diagnosed Petitioner with an infection. Importantly, that chronology persisted even after her MPA was properly diagnosed. Petitioner noted to treaters during her hospitalization in January of 2015 that her cold symptoms started following her flu shot. Despite this information, none of her treaters identified her flu vaccine as causal or reassessed her prior URI diagnosis. While petitioners do not need to present evidence of causation from treaters, the assertion by Petitioner's experts in this case that her treaters were incorrect does highlight their opinions and potentially contradicts the pathology asserted in this case. In the face of contemporaneous medical records from multiple treaters, including general practitioners to surgeons that consistently diagnose Petitioner with a URI, I do not find that she has presented preponderant evidence to rebut her URI diagnosis.

Dr. Oddis also identified Petitioner's URI as the most likely cause of Petitioner's MPA. However, Respondent's burden to provide preponderant evidence of alternative causation only arises when Petitioner presents evidence to establish a prima facie case. Petitioner's inability to present sufficient evidence of a causation theory means that the burden never shifts to Respondent in this case.

c. Timing: *Althen* Prong Three

Petitioner did not identify an appropriate timeframe for the onset of MPA symptoms caused by the flu vaccine. Dr. Lally's opinion that Petitioner's symptom onset timeline establishes a clear relationship is a conclusion that lacks evidentiary support. The case study that Petitioner presented does describe a timeline of approximately one week, and that could be consistent with Petitioner's account. Molecular mimicry is commonly expected to occur within days to weeks of exposure to the mimic. In this case, Petitioner's symptoms, whatever the cause, occur within proximity to her vaccination. I cannot conclude that Petitioner's alleged timeframe is consistent without more context. However, I can find that Petitioner has presented preponderant evidence that her symptoms developed within days to one week of vaccination.

VI. Conclusion

Petitioner has experienced an immeasurable loss, and I have reviewed the entire record in an effort to understand what happened to her. In this case, Petitioner has been unable to present preponderant evidence of a causation theory that links the flu vaccine to MPA or to apply said

theory to her medical history and establish causation in her case. Petitioner's URI diagnosis is also compelling evidence of a stronger immunogenic response that may be responsible for her immune system disorder. Consequently, Petitioner has not met her burden to establish that but-for her flu vaccination, she would not have developed MPA. Therefore, her claim must be dismissed.

IT IS SO ORDERED.

s/Herbrina D. Sanders
Herbrina D. Sanders
Special Master